syphilis shall be treated with either penicillin alone or penicillin and bismuth.

CONCLUSIONS

1. A middle-aged white female confirmed alcoholic, developed medical shock with a fatal outcome following neoarsphenamine therapy in the treatment of her syphilis.

2. Suggestions and recommendations are made as to the diagnosis and management of medical shock following neoarsphenamine therapy.

3. It is recommended that syphilis in a confirmed alcoholic be treated with penicillin alone or with penicillin and bismuth, but not with an arsenical.

Great appreciation is expressed by the authors of this article to Dr. D. E. H. Cleveland, Vancouver, and Dr. D. H. Williams, Vancouver, for valuable advice and assistance in preparation of this article.

BIBLIOGRAPHY

1. STOKES, BEERMAN, INGRAHAM: Modern Clinical Syphilology, W. B. Saunders Co., Philadelphia and London, 1944.
2. MOORE, J. E.: The Modern Treatment of Syphilis, Charles C. Thomas, Springfield, Ill., 1941.
3. WEINBERG, T.: *Am. J. Syph., Gonor. & Ven. Dis.*, 21: 376,, 1937.
4. ORR, H.: *Brit. J. Dermatol. & Syph.*, 45: 58, 1933.
5. ATCHLEY, D. W. AND LOEB, R. F.: *Med. Clin. North Am.*, 17: 1379, 1933-34.
6. PHELPS, R. JR.: *U.S. Nav. M. Bull.*, 22: 217, 1925.
7. HELFORS, A.: *Med. Klin.*, 29: 117, 1933.
8. HIRANO, N.: *Kitasato Arch. Int. Med.*, 3: 1, 1919.
9. REID, W. D.: *J. Am. M. Ass.*, 84: 883, 1925.
10. WILSON, F. N., WILE, U. J., WISHART, S. W. AND HERRMANN, G. R.: *Proc. Soc. Exper. Biol. & Med.*, 23: 275, 1926.
11. ORR, H.: Personal communication.
12. *Idem*: *Proc. Ninth International Dermatol. Cong.*, Budapest, 1935.

VIRUS INFECTIONS OF THE CENTRAL NERVOUS SYSTEM*

A. J. Rhodes, M.D., F.R.C.P.(Edin.)

Connaught Medical Research Laboratories and School of Hygiene, University of Toronto, Toronto, Ont.

VIRUS infections of the central nervous system present a major problem in many parts of the world and specially in North America. The most frequently diagnosed nervous diseases of virus etiology in this continent are poliomyelitis, equine encephalomyelitis, St. Louis encephalitis, lymphocytic choriomeningitis, rabies, and meningitis associated with mumps or herpes. With present facilities for rapid air travel it is quite possible, however, for cases of nervous disease contracted in any part of the world to be seen by physicians in Canada and America. Unless such physicians are well acquainted with the whole range of neurotropic virus diseases, mistaken diagnoses may be made, and valuable specimens for laboratory tests may not be collected. Furthermore, such cases may come to be reported in the literature as suffering from "a hitherto undescribed infection", when in reality they are suffering from a disease well-recognized elsewhere.

My object in this paper is to mention briefly the recognized virus infections of the central nervous system that have been described in all parts of the globe; this will be done by discussing a simple scheme into which these infections can be classified. Laboratory tests are available for the diagnosis of many of these diseases; the present scope of these investigations has recently been outlined elsewhere (Rhodes, 1948).

At least 35 antigenically distinct strains of viruses can cause an infection of the central nervous system in man. Many of these viruses differ widely one from another in biological properties, but others are closely related. Of recent years, a number of studies have been carried out on the antigenic relationships of neurotropic viruses, and this information enables us to build up a reasonable classification. The methods used in these studies include complement fixation and virus neutralization tests, and cross resistance tests in immunized laboratory animals. However, a classification based on antigenic structure is of little value to the clinician, who requires something more practical, something that will help particularly in the differential diagnosis of an obscure case of nervous disorder of presumed viral origin. Accordingly, I have fitted the various infections of the central nervous system into a mainly clinical, pathological, and epidemiological framework, but it should be borne in mind that the primary basis of subdivision is antigenic structure.

The first and most obvious differentiation is between (*a*) those viruses in which nervous involvement is only secondary to a primary localization of the virus elsewhere in the body; and (*b*) infections due to the neurotropic viruses proper, where the primary localization of the virus is in the central nervous system. We shall concern ourselves, in this paper, chiefly with the neurotropes proper.

* Portion of an address given to the Montreal Neurological Society, January 28, 1948.

A. Diseases Where Nervous Involvement is Secondary to Primary Localization Elsewhere in Body

Encephalitis, meningo-encephalitis, or more diffuse involvement may arise as a complication of several virus diseases of man: dengue; glandular fever; herpes febrilis (simplex); herpes zoster (zona); infective hepatitis; influenza; lymphogranuloma inguinale; measles; mumps; rubella; sand-fly fever; vaccinia; variola; varicella.

The clinical evidence of nervous involvement is usually apparent within one or two weeks after the onset of the illness. Occasionally, as in mumps, nervous involvement may appear before the primary lesions can be detected. Rarely, the nervous involvement may appear to be the only manifestation of infection, although here it would seem probable that a primary focus is present in the upper respiratory tract.

Histologically, the lesions produced by certain of these viruses are practically identical, and perivascular demyelination is frequently found. It must be emphasized, however, that there are few reports of the histological picture produced by many of the above agents. It is to be noted that these viruses do not cause epidemics of nervous disease, and the occurrence of nervous involvement is essentially an unexpected complication, presumably due to some peculiar combination of circumstances in the particular host. These viruses, with the exception of that of herpes febrilis, do not behave as true neurotropic agents on inoculation in experimental animals.

B. Diseases Where Nervous Involvement is Primary — True Neurotropic Infections

There are a large number of viruses that can be properly described as "neurotropic". In man, the characteristics of a neurotropic infection are that the presenting symptoms and signs are due to involvement of the brain or cord; other organs are not primarily involved. After entry to the human body by the respiratory tract, gastro-intestinal tract, or skin, neurotropic viruses reach the C.N.S. by a variety of routes. Some may spread along the axons of superficially situated nerve fibres (*e.g.*, poliomyelitis). Others may spread along the axons of more deeply situated nerves (*e.g.*, rabies). In other cases, virus is implanted by an insect bite in the blood stream, and after circulating localizes in the C.N.S. (*e.g.*, St. Louis, Japanese, and equine encephalitis). In experimental animals, neutrotropic viruses rapidly reach the C.N.S. after inoculation by peripheral routes, and titration experiments show that the highest concentration of virus is in the brain or cord. Spread from the portal of entry may be by axons, or by the blood stream.

The primary neurotropic virus infections can be subdivided into several groups as follows:

1. Diseases where involvement is mainly meningeal.
2. Diseases where the anterior horn cells are mainly involved (poliomyelitis).
3. Infection by the rabies group of viruses.
4. Encephalitis lethargica (von Economo).
5. Mosquito-borne encephalitides.
6. The equine encephalomyelitis group.
7. Tick-borne encephalitides.
8. Epidemic encephalitides of unidentified etiology.

These various groups will now be discussed individually.

1. *Diseases where involvement is mainly meningeal*: (*a*) Lymphocytic choriomeningitis. (*b*) Pseudolymphocytic choriomeningitis. (*c*) Durand's disease. (*d*) Swineherd's disease (eruptive meningo-typhoid, *maladie des porchers*).

These infections, of which the first is the best known, present clinically as a "serous" meningitis, having a sudden onset and short benign course. Numerous lymphocytes are found in the cerebrospinal fluid. Lymphocytic and pseudolymphocytic meningitis are caused by closely related neurotropic viruses, and it seems that infection is usually contracted from house mice, the normal carriers of the virus. The two viruses are antigenically distinct. Durand's virus has only been isolated once (in Africa), and is probably of no general importance. Swineherd's disease is a prevalent infection in parts of Switzerland, France, and Italy, and appears to be contracted by handling sick pigs. The infection has been transmitted by means of filtrates of human blood. The virus has not been studied as regards its antigenic structure.

2. *Diseases where the anterior horn cells are mainly involved.*—Because of its characteristic primary attack on the ganglionic nerve cell, especially the anterior horn cells of the spinal cord, poliomyelitis virus is most suitably classified in a category by itself. A few years ago, poliomyelitis virus was thought to cause natural infection of man alone, and experimentally to be transmissible only to the monkey. Of recent years, however, it has become evident that there is a poliomyelitis

group of viruses, containing the following members (see Gard, 1943):

(*a*) Human poliomyelitis virus transmissible experimentally only to monkeys.

(*b*) Human poliomyelitis virus transmissible experimentally to mice, hamsters, cotton rats, and guinea-pigs, *i.e.*, the Lansing, SK, and MEFI strains (Armstrong, 1939; Trask, Vignec, and Paul, 1938 *a*, *b*; Schlesinger, Morgan, and Olitsky, 1943).

(*c*) Miscellaneous strains such as the MM, recovered from animal and non-human sources (Jungeblut and Dalldorf, 1943, 1946; Toomey, Takacs, and Weaver, 1945).

(*d*) Mouse poliomyelitis (Theiler, 1934, 1937, 1941).

Only the first two infect man. The great bulk of strains of poliomyelitis virus isolated from the C.N.S., naso-pharynx, or stool of cases of abortive or paralytic infection can only be transmitted to the monkey. So few strains can be transmitted to rodents that this is of little practical significance.

The strains that have been isolated from human beings, that are transmissible to rodents, share antigenic components with the monkey-pathogenic strains. It is almost certain that there are antigenic varieties of human poliomyelitis strains, analogous, for example, to the types and strains of influenza virus. For technical reasons, it has not yet proved possible to investigate this problem; an enormous number of monkeys would be required, and the work could not be undertaken by one laboratory. Yet, much of our understanding of poliomyelitis problems depends on a knowledge of whether or not there are several antigenic varieties of virus, that may not give cross immunity one to another.

The disease of mouse poliomyelitis is of considerable interest. This virus, of which a number of different strains exist, is carried by the majority of adult laboratory mice and is excreted in their stools. In a small number of cases, in young animals, the virus causes necrosis of the anterior horn cells, with the production of flaccid paralysis. We have here an endemic infection transmitted by the oral route, in which only occasionally does the young susceptible non-immune animal develop paralysis (see also, Olitsky, 1939). Although it is tempting to argue by analogy, it is probably unjustifiable to draw too many conclusions regarding human poliomyelitis from the mouse disease. It is a matter for speculation whether certain types of polyradiculitis or polyneuritis (*e.g.*, Guillain-Barré syndrome) may not be due to a virus allied to that of poliomyelitis, but there is no experimental evidence in support.

3. *The rabies group of viruses.*—Rabies attacks many animals and man; and the essential characteristics of the disease are similar in different hosts. A number of different strains of rabies street virus exist. (*a*) *Renforcé* strains. (*b*) Trinidad rabies virus (also *mal de caderas* in bovines). (*c*) Ordinary strains of street virus. (*d*) *Oulou fato* virus.

The majority of these street strains can be transformed, by passing in series through the brains of rabbits, into the laboratory virus known as *virus fixe* or fixed virus. *Renforcé* strains have an unusually high virulence for laboratory animals, and infections are characterized by a short incubation period. It has not been settled whether these strains necessarily cause a more fulminant infection in man, but there is probably no correlation between the clinical picture in naturally infected man and experimentally infected rabbits. The Trinidad virus differs considerably from other strains, in that it is spread by vampire bats (*Desmodus rotundus murinus*), and in man causes an ascending Landry-like type of paralysis. The same virus causes rabies of cattle (*mal de caderas*). The virus of indigenous mad dog disease of Africa (*oulou fato*) is of very low infectivity to experimental animals, and probably man also.

4. *Encephalitis lethargica* (*von Economo*).—This disease had epidemic prevalence in the 1920's, but apparently is now seldom seen. Many investigations were made on the etiology, but no virus was isolated that was generally accepted as the causal agent. French workers isolated the virus of herpes febrilis from a few cases, and claimed that it was the causal agent. Many others, however, failed to isolate this virus, which at any rate is known to be commonly carried by many adults without the production of disease. Of recent years it has been shown definitely that the virus of herpes febrilis can cause encephalitis, but it seems that clinically and pathologically herpetic encephalitis can be distinguished from encephalitis lethargica. At the present, the only possible conclusion is that the causal agent of encephalitis lethargica awaits discovery. The disease presents distinctive clinical, histological, and epidemiological features, justifying classification in a category of its own.

5. *Mosquito-borne virus encephalitis. — St. Louis encephalitis,* which is fairly widely distributed over the United States, is caused by a readily isolated neurotropic agent that is spread by mosquitoes such as *Culex tarsalis.* The virus causes infection also of domestic animals and chickens. It seems probable that the common cycle of the virus occurs in domestic animals and chickens, the transmitting agents being mosquitoes; chicken mites also transmit the infection (see Hammon and Reeves, 1945).

Japanese (Type B) encephalitis, which occurs throughout Japan and in the seaboard districts of China and Far Eastern Russia is also spread by mosquitoes. Until a few years ago, the disease frequently recurred in the summer months in Japan, involving hundreds of persons. Of recent years, for some unexplained reason, the usual picture has been of sporadic cases.

A number of other viruses have been isolated by yellow fever workers in Africa and S. America, and some, such as the *West Nile* virus, can certainly infect man. Hammon and Reeves have isolated a *California* virus that probably causes encephalitic infection in man. Investigations have shown that the Japanese, St. Louis, and West Nile viruses share antigenic components; this group can be differentiated from the virus of equine encephalitis (Kasahara, Yamada, and Hamano, 1937; Smithburn and Jacobs, 1942; Casals, 1944; Lennette and Koprowski, 1946).

6. *The equine encephalomyelitis group of viruses.*—Equine encephalomyelitis is also mosquito-borne, but it is more convenient to discuss this group of infections separately, as the equine viruses are distinct antigenically from the Japanese, St. Louis, and West Nile group. The following are the antigenically distinct members of the equine encephalomyelitis group: (*a*) European Borna disease of horses; (*b*) Russian equine encephalitis; (*c*) North American equine encephalomyelitis, Eastern type; (*d*) North American equine encephalomyelitis, Western type; (*e*) Venezuelan equine encephalomyelitis virus.

Only the last three are thought to infect man. The virus of Borna disease is antigenically distinctive (Howitt and Meyer, 1934), as is that of Russian encephalitis (Howitt, 1935, 1937). The Western and Eastern types of North American equine virus are serologically distinct, although there is some sharing of common antigens (Howitt, 1935, 1938; Records and Vawter, 1935; Shahan and Giltner, 1935; Havens *et al.,* 1943). A strain of virus closely resembling the Eastern type occurs in Brazil, and may be described as the Brazilian strain of the Eastern type (Carneiro, 1937). An Argentinian strain of the Western type has also been described (Rosenbusch, 1934). Neither the Brazilian nor the Argentine strains are thought to infect man. The Venezuelan virus is antigenically distinct from both the North American types (Beck and Wyckoff, 1938). It has been described also in Colombia (Soriano Lleras and Figueroa, 1942). Normally, the virus only causes infection of horses, but human disease has occurred in Trinidad (Gilyard, 1944). A number of laboratory infections have been reported (Casals, Curnen, and Thomas, 1943; Lennette and Koprowski, 1943).

7. *Tick-borne encephalitis.*—Two types of encephalitis are known to be spread by ticks: (*a*) Russian Far-Eastern spring-summer encephalitis. (*b*) Louping-ill. The Russian virus is spread by *Ixodes persulcatus* and perhaps other ticks, and involves man. There is a severe Eastern form of the disease, and a milder Western form (see Silber and Soloviev, 1946). The disease louping-ill is primarily one of sheep. It has been most studied in Scotland, but probably also occurs in Russia. The Russian encephalitis and louping-ill viruses are closely related (Casals and Webster, 1943, 1944; Casals, 1944). (*c*) Colorado tick fever, although it appears to be mainly a blood infection, has symptoms suggestive of nervous involvement.

8. *Epidemic and sporadic encephalitis of unidentified etiology.*—Various outbreaks of encephalitis have been reported in which it appeared likely that a virus was responsible. However, for various reasons no special studies could be made. For example, such outbreaks have been reported from Central Africa (Charters, 1940; Berney and Gelfand, 1946); the Argentine (Valdes, 1943); Brazil (Di Lascio, 1943); Germany (Gildemeister and Haagen, 1940); India (Chatterji, Gupta, and De, 1945); Sweden (Möller, 1939); and Texas (Woodland and Smith, 1942). A particularly interesting occurrence was that of Australian X disease, from which no definite virus was recovered, although the histological appearances of the disease were not unlike those characteristic of louping-ill.

Finally, a few sporadic cases of encephalitis have been reported in which it appears probable that a specific virus was responsible: "inclusion" encephalitis is characterized by the presence of herpetic type intranuclear inclusions in the ganglionic cells of the cortex (Brain, 1943; Greenfield, 1943; Russell, 1943); a disease occurring in Russia has been named acute primary hæmorrhagic meningo-encephalitis, and a virus has been isolated (Margulis, Soloviev, and Shubladze, 1944); Horan *et al.* (1944) described two fatal cases in troops in N. Australia probably due to a neurotropic virus.

SUMMARY

The numerous viruses that can cause an infection of the central nervous system are discussed and classified into groups on the basis of antigenic structure and other properties.

BIBLIOGRAPHY

1. ARMSTRONG, C.: *Pub. Health Rep.*, **54**: 1719, 1939.
2. BECK, C. E. AND WYCKOFF, R. W. G.: *Science*, **88**: 530, 1938.
3. BERNEY, B. P. AND GELFAND, M.: *East African Med. J.*, **23**: 174, 1946.
4. BRAIN, R.: *Proc. Roy. Soc. Med.*, **36**: 319, 1943.
5. CARNEIRO, V.: *Arch. Inst. Biol.*, **8**: 115, 1937.
6. CASALS, J.: *J. Exper. Med.*, **79**: 341, 1944.
7. CASALS, J., CURNEN, E. C. AND THOMAS, L.: *J. Exper. Med.*, **77**: 521, 1943.
8. CASALS, J. AND WEBSTER, L. T.: *Science*, **97**: 246, 1943.
9. *Idem*: *J. Exper. Med.*, **79**: 45, 1944.
10. CHARTERS, A. D.: *East African Med. J.*, **16**: 459, 1940.
11. CHATTERJI, J. R., GUPTA, N. AND DE, M. N.: *Indian M. Gaz.*, **80**: 285, 1945.
12. DI LASCIO, A.: *Neurobiologia*, **6**: 202, 1943.
13. GARD, S.: *Acta. med. Scandinav., supp.* 143, 1943.
14. GILDEMEISTER, E. AND HAAGEN, E.: *Deutsche med. Wchnschr.*, **66**: 1358, 1940.
15. GILYARD, R. T.: *Bull. U.S. Army Med. Dept.*, No. 75, 96, 1944.
16. GREENFIELD, J. G.: *Proc. Roy. Soc. Med.*, **36**: 391, 1943.
17. HAMMON, W. M. AND REEVES, W. C.: *Am. J. Pub. Health*, **35**: 994, 1945.
18. HAVENS, W. P. JR., WATSON, D. W., GREEN, R. H., LAVIN, G. I. AND SMADEL, J. E.: *J. Exper. Med.*, **77**: 139, 1943.
19. HORAN, J. P., JOHNSTON, G. A. W., HALLIDAY, J. H., O'BRIEN, J. AND HURST, E. W.: *Brain*, **67**: 93, 1944.
20. HOWITT, B. F.: *J. Immunol.*, **29**: 319, 1935.
21. *Idem*: *J. Immunol.*, **33**: 235, 1937.
22. *Idem*: *J. Infect. Dis.*, **63**: 269, 1938.
23. HOWITT, B. F. AND MEYER, K. F.: *J. Infect. Dis.*, **54**: 364, 1934.
24. JUNGEBLUT, C. W. AND DALLDORF, G.: *Am. J. Pub. Health*, **33**: 169, 1943.
25. *Idem*: *Am. J. Hyg.*, **43**: 49, 1946.
26. KASAHARA, S., YAMADA, R. AND HAMANO, R.: *Kitasato Arch. Exper. Med.*, **14**: 229, 1937.
27. LENNETTE, E. H. AND KOPROWSKI, H.: *J. Am. M. Ass.*, **123**: 1088, 1943.
28. *Idem*: *J. Immunol.*, **52**: 235, 1946.
29. MARGULIS, M. S., SOLOVIEV, V. D. AND SHUBLADZE, A. K.: *Am. Rev. Sov. Med.*, **1**: 409, 1944.
30. MÖLLER, F.: *Nord. med.*, **4**: 3215, 1939.
31. OLITSKY, P. K.: *Proc. Soc. Exper. Biol. & Med.*, **41**: 434, 1939.
32. RECORDS, E. AND VAWTER, L. R.: *J. Am. Vet. M. Ass.*, **86**: 773, 1935.
33. RHODES, A. J.: *Manitoba Med. Rev.*, March, 1948.
34. ROSENBUSCH, F.: *Z. Infekt. Kr. Haustiere*, **47**: 48, 1934.
35. RUSSELL, D. S.: *Proc. Roy. Soc. Med.*, **36**: 319, 1943.
36. SCHLESINGER, R. W., MORGAN, I. M. AND OLITSKY, P. K.: *Science*, **98**: 452, 1943.
37. SHAHAN, M. S. AND GILTNER, L. T.: *J. Am. Vet. M. Ass.*, **86**: 764, 1935.
38. SILBER, L. A. AND SOLOVIEV, V. D.: *Am. Rev. Sov. Med.*, Special supplement, 1946.
39. SMITHBURN, K. C. AND JACOBS, H. R.: *J. Immunol.*, **44**: 9, 1942.
40. SORIANO LLERAS, A. AND FIGUEROA, L.: *Bol. Inst. nac. Hig. Samper Martinez, Bogota*. No. 8, p. 3, 1942.
41. THEILER, M.: *Science*, **80**: 122, 1934.
42. *Idem*: *J. Exper. Med.*, **65**: 705, 1937.
43. *Idem*: *Medicine*, 20: 443, 1941.
44. TOOMEY, J. A., TAKACS, W. S. AND WEAVER, H. M.: *Am. J. Dis. Child.*, **70**: 293, 1945.
45. TRASK, J. D., VIGNEC, A. J. AND PAUL, J. R.: *Proc. Soc. Exper. Biol. & Med.*, **38**: 147, 1938*a*.
46. *Idem*: *J. Am. M. Ass.*, **111**: 6, 1938*b*.
47. VALDES, J. M.: *Arch. argent. de pediat.*, **14**: 263 (See *J. Am. M. Ass.*, **124**: 810, 1944.)
48. WOODLAND, J. C. AND SMITH, E. M.: *J. Am. M. Ass.*, **120**: 358, 1942.

A MODERN APPROACH TO PSYCHOANALYSIS*

Norman Viner, M.D.

Montreal, Que.

BY way of introduction some historic background is necessary, even if it is very slight. During the first thousands of years of civilization we had religion, ethics, superstition and philosophy, the latter mainly in the form of metaphysics. Mind and matter, or body and soul, were rigidly differentiated and whatever mental treatment there was, when not exhibited in the form of exorcism or incantation, was applied in a physical manner. The poor victim was subjected to beatings, chains, breaking on the wheel, casting into hot or cold water or witch-burning. This was not only for what we consider the psychotic, but for the neurotic as well, if they showed so little restraint as to talk or behave too much beyond the accepted norm. It was only the final century of that period that began to show a dawning humanity and understanding, when some degree of mercy was accorded to the poor wretches, as in Paris under Pinel, in York, England, and in Philadelphia, in particular, where the Quakers decided that these hapless creatures should be "treated as men and brethren".

And so we come to the middle of last century, when with the beginnings of scientific research, the industrial revolution and the progressive writings of Chambers, Darwin, Wallace and Huxley, and the evolution of the theory of evolution, that a spirit of crass materialism, or should I say of physicism, began to dominate the intellectual field to the exclusion of belief, so that the defenders of the latter were driven to the use of the opposing slogans of "What is matter? Never mind". "What is mind? No matter".

* Given before the Montreal Psychiatric Society, March 2, 1948.